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Exploring the Contribution of Pharmacists in Addressing the Opioid Crisis through Naloxone Prescriptions and Pharmacist-Led Interventions

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Abstract

The opioid epidemic in the United States continues to take the lives of many individuals, with overdoses continuing to rise every year. Naloxone is an opioid antagonist that is efficacious in temporarily reversing opioid overdoses. Pharmacists play an important role in the accessibility and education of naloxone in both the community and health system settings. Recent efforts, such as co-dispensing naloxone with opioid prescriptions, naloxone training programs, and approval of naloxone to be over-the-counter, have been implemented in hopes to better control the opioid epidemic. Despite the efforts to make naloxone more accessible, there are still some barriers to overcome such as lack of training, cost, stigma, and patient refusal. This review aims to explore the contributions pharmacists have made thus far and define the barriers that still have to be resolved.

Keywords

Naloxone, Narcan, Opioid Crisis, Opioid Epidemic, Pharmacy, Pharmacist, Interventions

1. Introduction

The opioid epidemic in the United States is a serious issue that continues to take the lives of many individuals. Despite current efforts in place, opioid use and misuse continue to increase. Current data indicate the immediate need for healthcare and public health approaches to reduce the amount of opioid overdoses [1]. Different types of interventions are used by pharmacists to address the opioid cri-

sis in the U.S. Some of these efforts include de-prescribing, medication management programs, and prescription drug monitoring programs (PDMPs) [2] [3]. De-prescribing is the act of reducing the dose or stopping a medication that does not provide therapeutic benefit to the patient or could cause harm. A patient's therapeutic regimen can change over time, and medication reviews should be done periodically to identify possible medications that can be de-prescribed to reduce the risk of adverse events and reduce medication burden [4]. Implementation of drug assistance programs has increased, however, more drastic measures need to be taken nationwide.

An emerging strategy of dispensing naloxone with opioid prescriptions is an important intervention that pharmacists are implementing. Naloxone is a life-saving medication that temporarily reverses the effects of an opioid overdose. Naloxone is becoming more readily available for dispensing in pharmacy practice settings, either by allowing pharmacists to prescribe naloxone or offering over-the-counter naloxone, and pharmacists play a crucial role in connecting patients with naloxone and the proper education on naloxone. Pharmacists bridge the gap to access these medications to patients, and they are often the last healthcare professionals patients interact with before receiving opioids.

Recent legal authorizations at the state and federal level have eased the dispensing of naloxone in pharmacies, however, there are still barriers to dispensing naloxone that need to be addressed. Potential barriers include time limitations, inadequate pharmacist training, and the cost of naloxone [5] [6]. Taking appropriate measures to overcome these barriers would only help the goal of getting naloxone into more patients' hands.

2. Opioid Epidemic

Opioid overdoses have hit a record high in the past few years. The Center for Disease Control and Prevention (CDC) shows fatal overdoses have only been increasing, reversing progress that was made in 2018 [7]. It has been suggested that COVID-19 suppressing opioid use disorder management systems have made the problem worse [7] [8]. Social isolation can make it harder for people with substance use disorder to manage their condition because they are not able to interact with peers and get the support that they need from friends and family. Also, it makes it less likely that they will be around others in the case of an overdose. Another driving factor for an increase in overdose deaths during COVID-19 is that many outpatient facilities that provide in-person services, such as needle exchanges, naloxone distribution, and medication-based therapy, can no longer operate [7]. The trend of opioid overdose deaths from 1999 to 2021 is shown in **Figure 1**. There are high levels of agreement amongst healthcare professions that there is a need within our community to address the opioid crisis due to worsening statistics that correlate with worsening clinical outcomes [9].

Among healthcare professions that are able to contribute to the goal of reducing the number of fatal opioid overdoses, pharmacists are at the frontline when

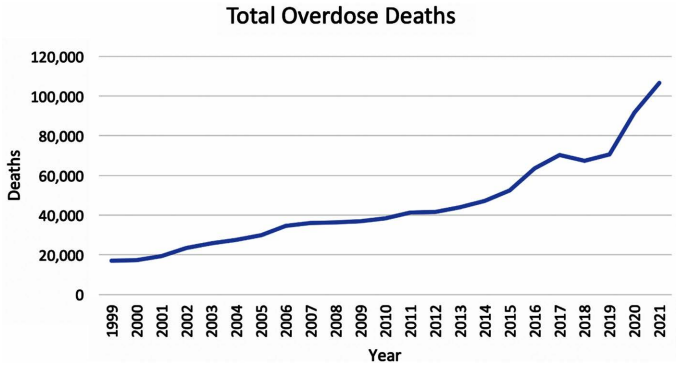

Figure 1. Total deaths from an opioid overdose between the years of 1999 and 2021, with the majority of deaths being from synthetic opioids such as fentanyl [7].

it comes to giving patients access to opioids. There are many roles that pharmacists play within the opioid crisis; several examples include interventions aimed at preventing misuse and improving patient safety, screening and monitoring opioid prescribing and usage, assisting in the recovery and rehabilitation process of patients with opioid use disorder (OUD), and collaboratively managing OUD with pharmacotherapy agents [10]. Among the many roles and programs implemented by pharmacists, an important one that remains is the prescribing and dispensing of naloxone to patients at risk for opioid overdose. Risk factors for opioid overdose are listed in **Table 1** along with current opioids in **Table 2**. Although an important pharmacist-led intervention, the prescribing and dispensing of naloxone is still negatively affected by the potential barriers of time limitations in pharmacy workflow, inadequate pharmacist training, and the cost of naloxone to patients if a patient's insurance does not cover it [5] [6].

3. Naloxone

Naloxone, also dispensed as brand name Narcan, is an opioid antagonist that works on the mu, kappa, and sigma receptors [1] [13]. Naloxone reverses respiratory and central nervous system depression, commonly known as an opioid overdose [1]. An opioid overdose can be identified if the patient has loss of consciousness, slowed breathing, pinpoint pupils, pale or cold skin, or slowed heart rate [14]. Any individual who identifies these signs in a person should immediately call 911 and administer naloxone, even if it is not a confirmed overdose since there are no adverse effects if you administer it in a non-overdose case. An individual experiencing respiratory depression may have trouble breathing or stop breathing. Many randomized controlled trials have proven the efficacy of at-home naloxone to temporarily reverse an overdose [15] [16].

Legal aspects of naloxone prescribing are similar to any other prescription medication. All 50 states have passed legislation regarding easier access to naloxone. Most states allow pharmacists to prescribe naloxone without physician authorization if the patient meets criteria that are specific to each state [17]. The cost of naloxone varies by formulation, distributor, and patient insurance [13].

Table 1. Factors that put patients at an increased risk of an opioid overdose [11] [12].

Risk Factors for Opioid Overdose
Concurrent use of benzodiazepines, muscle relaxers, and/or alcohol
Poly-pharmacy patients
Receiving a methadone prescription
History of opioid addictions or other substance use disorders
High-dose opioid prescription
History of injection drug use

Table 2. List of current opioids including prescription, illegal, and semi-synthetic/synthetic opioids and opioid antagonists. Several brand names are stated and may include combination products such as oxycodone/acetaminophen (Percocet).

Prescription Opioids	Illegal Opioids	Semi-Synthetic & Synthetic Opioids	Opioid Antagonists
Morphine	Heroin	Fentanyl	Naloxone (Narcan)
Codeine	Carfentanil	U-47700	Naltrexone
Oxycodone (OxyContin, Percocet)		MT-45	Methylnaltrexone
Hydrocodone (Vicodin, Lortab, Norco)		3-Methylfentanyl	Nalmefene
Fentanyl		Acetylfentanyl	
Methadone		Butyrfentanyl	
Hydromorphone (Dilaudid, Exalgo)		Furanylfentanyl	
Oxymorphone (Opana)		Desomorphine (Krokodil)	
Meperidine (Demerol)		Thebaine	
Tramadol			
Tapentadol (Nucynta)			
Buprenorphine (Suboxone, Subutex)			
Pentazocine (Talwin)			
Levorphanol (Levo-Dromoran)			
Butorphanol			
Dihydrocodeine			
Levomethadyl Acetate (LAAM)			
Dextropropoxyphene			
Diphenoxylate (Lomotil)			
Paregoric			
Alfentanil (Alfenta)			
Rremifentanil (Ultiva)			
Sufentanil			
Dezocrine			
Anileridine			
Pethidine (Demerol)			

Pharmacists are able to determine costs and insurance coverage in addition to initiating the prescription of naloxone. Changes in laws at both federal and state levels have aimed to expand the use of naloxone for emergency treatment situations. The Comprehensive Addiction and Recovery Act (CARA) is one example of a federal law put in place as a necessary, coordinated effort to address the opioid crisis [18]. Outlined in new legislation, pharmacist prescribing of naloxone is a harm reduction strategy intended to save lives from the immediate treatment of an overdose. Increasing the availability of naloxone is an important community health measure that has potential to reduce the number of fatal overdoses.

The regulatory reasons behind the legal change allowing pharmacists to prescribe naloxone stem from the growing need to address the opioid overdose epidemic that has been affecting many countries, particularly the United States. With overdoses continuing to rise, the opioid epidemic has been an increasing public health emergency despite current efforts made to decrease this number. The implementation of more flexible regulations is necessary to combat the opioid crisis. Allowing pharmacists to prescribe naloxone provides easier accessibility to education and training in all patient populations in addition to providing naloxone [18]. Community pharmacies are located where other healthcare facilities and services might be limited. Pharmacists in lower income community settings provide professional healthcare access to those who may not receive adequate health care anywhere else [19]. Reducing barriers to obtain naloxone in lower income communities is an important implementation that allows for quick access to naloxone without having to see a physician first [5]. Pharmacists' prescribing of naloxone is also appropriate and beneficial to patients because pharmacists are proficiently trained to provide education on an opioid overdose and the administration of naloxone. The accessibility and knowledge of pharmacists make them excellent candidates for frontline workers in the opioid epidemic [18] [19]. Pharmacist prescribing of naloxone is a harm reduction strategy intended to save lives from the immediate treatment of an overdose.

4. Pharmacist Contributions in Community Settings

Community pharmacists across the U.S. have participated in naloxone distribution programs that aim to dispense naloxone to patients taking opioids [20] [21]. Clinical and legal environments have become more conducive to the availability and dispensing of naloxone through community pharmacies [13]. Although prescribing opportunities are rising, it is equally as important for pharmacists to be prepared for screening, monitoring, and educating patients.

In order for naloxone to be dispensed appropriately, patient screening has been implemented into community pharmacy workflows. Most screening programs revolve around finding patients with risk factors for opioid overdose. Identifying high risk patients may require additional screening efforts. One study showed that most pharmacies (83%) that were able to identify high risk patients were

located either within or in close proximity to hospitals, methadone clinics or HIV clinics [12]. This collaborative system makes it easier for pharmacists to identify these patients, however, other screening protocols must be implemented in community pharmacies that do not have this relationship with other healthcare providers. Many states are emphasizing co-prescribing or co-dispensing of naloxone to patients that are at an increased risk of an opioid overdose, such as those taking high doses of opioids, are concomitantly taking benzodiazepines, and have a history of respiratory conditions (*i.e.* COPD) [22]. The CDC released an opioid prescribing guideline in 2016 that recommends a naloxone co-prescription in certain patient populations [23]. Co-prescribing recommendations such as these have increased dispensed naloxone prescriptions when compared to previous restrictions [23] [24]. One cohort study demonstrated that naloxone co-prescribing was associated with approximately 7.75 times more dispensed naloxone [23]. With community pharmacists working the front lines of the opioid crisis, catching high risk individuals and co-prescribing naloxone has been an effective intervention to get naloxone in the hands of patients who may need it.

Providing education on naloxone and its administration is an imperative step when dispensing these at-home products. It is important for pharmacists to be adequately trained on this topic to ensure proper steps are taken pre- and post-administration. Many pharmacies have developed their own counseling techniques, although education documentation needs to be standardized.

5. Pharmacist Contributions in Health-System Settings

In addition to community pharmacists, pharmacists working in hospital and ambulatory care settings often have opportunities to collaborate with physicians. This more direct interaction of pharmacists and physicians eases conversations of naloxone prescribing. Collaborative care models involving pharmacists and physicians include Medication Therapy Management (MTM) and Collaborative Drug Therapy Management (CDTM) [25]. Interprofessional team based care has the opportunity to provide patient-centered care, although this is not often the case throughout healthcare systems. Pharmacy support can and should be viewed as an extension of the primary care team [25]. Pharmacists in hospital and ambulatory care settings have the opportunity to intervene and ensure patients are discharged with naloxone when opioids are also being prescribed.

One study evaluated opioid prescriptions for post-operative pain from common procedures and found that opioids are often over prescribed leading to excess opioids dispensed to patients [25] [26]. Along with de-prescribing efforts, pharmacists can suggest naloxone prescriptions and can provide proper education on naloxone administration. Identification of these high-risk patients is an intervention that can be overlooked by other healthcare professionals.

When compared to pharmacists that practice in a community setting, health-system pharmacists have additional and unique opportunities to ensure nalox-

one is dispensed to appropriate patients. The efforts of community and health-system pharmacists combined have the potential to reduce opioid overdoses in patient populations at risk.

6. Outcomes of Pharmacist Contributions

Pharmacist interventions across practice settings have the opportunity reduce harm. Implementation of naloxone education programs and the increased accessibility of over-the-counter naloxone can help reduce opioid overdose mortality. Pharmacists are the last point of contact for high overdose risk populations, and also to the general public. This puts them in an advantageous situation with the opportunity to educate the population on the risk of overdoses and provide training on naloxone.

One study showed that implementing overdose education and naloxone distribution (OEND) programs in Massachusetts significantly lowered fatal overdose rates [27]. In this study, community public health agencies provided OEND to potential overdose bystanders. The overdose education included identifying who is at high risk for an overdose, how to identify an overdose, and how to properly respond and administer naloxone. After completing the training and demonstrating proper understanding, participants were given two doses of intranasal naloxone. Even areas that had a low implementation rate of this program showed reduced rates compared to areas with no implementation. These programs included patients at risk for an overdose, as well as bystanders, and trained them to recognize signs of an overdose, seek help, and administer naloxone. Between 1996 and 2014, 644 sites in 30 states reported dispensing 152,283 naloxone kits to laypersons, and, out of that population, 26,463 reports were made for using naloxone for drug reversal [28].

Pharmacist's impacts on the whole population can help reduce mortality due to prescription and non-prescription opioid overdose. Bystanders, such as family members and drug-using partners have a strong interest in overdose prevention training and access to naloxone. Trained bystanders are similarly skilled compared to medical experts in identifying opioid overdoses and when naloxone is indicated [29]. Multiple studies have shown a greater survival rate, ranging from 83% - 100%, post-naloxone administration from people who have participated in some kind of opioid overdose prevention program [30]. In order to implement this training to the population, healthcare professionals, such as pharmacists, need to first be trained themselves. Many different studies utilize different techniques to train personnel, but the key features in all of them are didactic training, knowledge assessment, and to attend multiple bystander trainings themselves. This criterion can be compared to other life-saving programs, such as CPR certification, which contains the same key features.

Opioid overdoses are also a concern for illicit drug users. A survey that was conducted in San Francisco showed that 87% of injection drug users wanted a program that would train them to administer naloxone. It was also found that six

months after a naloxone training program, participants had a statistically significant decrease in injection frequency and an increase in entering treatment [31]. Pharmacists can have a significant impact on injectable drug users by helping the population become educated on naloxone and inadvertently decrease illegal opioid use and help them seek treatment [32].

The relationship between opioid overdose mortality due to increased accessibility to naloxone and education has been proven to be causative [31] [32]. If pharmacists continue to expand this access, we can further reduce the incidence of opioid related deaths and increase patient's chances for survival.

7. Barriers to Pharmacist Naloxone Dispensing

Although pharmacist prescribing of naloxone is implemented into state and federal laws to allow for easier accessibility to a live-saving medication, barriers have been identified across many studies [5] [6] [33] [34] [35]. Providing the opportunity for naloxone access to lower income and uninsured patients comes with the barrier of affordability for patients without drug insurance or limited drug coverage and in locations where naloxone is not publicly funded [6]. Time limitations and workload concerns are often barriers in fast-paced pharmacy environments. With other pharmacist responsibilities increasing, such as vaccinations, testing, and other prescriptive authorities, there may not be enough time to adequately identify and educate at-risk individuals. Without current procedures implemented into a pharmacy's workflow, pharmacists have reported time restraints on naloxone prescribing [33] [35]. Although the majority of pharmacies from one study perceived to have an area in their pharmacy that is HIPAA compliant, about 23% of pharmacies did not have a semi-private area for patient counseling [34]. This could contribute as a barrier to patient education.

Inadequate naloxone prescribing may also stem from lack of knowledge of prescriptive authority and training on the dispensation of naloxone. One study found that community pharmacists are not so likely to actually prescribe naloxone; Older pharmacists and males were less likely to prescribe naloxone [33] [34] [35]. Reasons for this may include a lack of training, lack of support from management, and/or the stigma surrounding opioid use and abuse from both patients and pharmacists. More standardized training could help ease the transition of the opioid epidemic stigma and allow for more comfortable patient-pharmacist interactions.

These barriers should be addressed across all pharmacy practice settings as it is essential to increase pharmacist participation in naloxone dispensing and interventions. Implementing training programs and providing education at the student pharmacist level would better prepare pharmacists to take action where they might not realize they are able to. Clinical, hospital, community, and PharmD graduate pharmacists all have unique and different opportunities to intervene and provide education. The different contributions of these various pharmacy practice settings make it challenging to take a definitive stance on which practicing

pharmacist is the most convenient to address the opioid crisis.

8. Conclusion

Pharmacists have helped with increasing the distribution of naloxone to patients prescribed opioids. Pharmacists act as the last healthcare professional between opioids and patients, and pharmacists have an important obligation to provide resources and education in order to slow the progress of the opioid epidemic. Legal opportunities have eased the process of pharmacists dispensing this life-saving medication, although there are current barriers that still exist. The contributions of pharmacists have only continued to increase, however, more actions need to be taken nationwide.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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